

CLAIMS

What is claimed is:

1. A method for directly identifying a candidate compound as a compound selected from the group consisting of an inverse agonist, a partial agonist and an agonist, to an orphan receptor, comprising the steps of:

(a) contacting a candidate compound with a constitutively activated orphan receptor;
and
(b) determining, by measurement of the compound efficacy at said contacted receptor, whether said compound is an inverse agonist, a partial agonist or an agonist of said receptor.

2. The method of claim 1 wherein the compound is determined to be an inverse agonist to said receptor.

3. The method of claim 1 wherein the orphan receptor is an endogenous constitutively activated orphan receptor.

4. The method of claim 1 wherein the orphan receptor is a non-endogenous constitutively activated orphan receptor.

5. The method of claim 1 wherein the orphan receptor is a G protein-coupled cell surface orphan receptor.

6. The method of claim 5 wherein the third intracellular loop of said orphan receptor comprises the following sequence:

X1BBHyX2

wherein X1 is an amino acid; B is a basic amino acid; Hy is a hydrophobic amino acid, and X2 is an amino acid.

7. The method of claim 6 wherein X1 is glycine.

8. The method of claim 6 wherein X1 is alanine.

9. The method of claim 6 wherein X1 is lysine.

10. The method of claim 6 wherein Hy is alanine.

11. The method of claim 6 wherein X2 is lysine.

5 12. The method of claim 6 wherein X2 is arginine.

13. The method of claim 6 wherein X2 is glutamic acid.

14. The method of claim 5 wherein the second intracellular loop of said orphan receptor comprises the following sequence:

XRY

10 wherein X can be any amino acid other than D.

15. The method of claim 6 wherein said sequence X1BBHyX2 is an endogenous sequence.

16. The method of claim 6 wherein said sequence X1BBHyX2 is a non-endogenous sequence.

17. The method of claim 14 wherein said sequence XRY is an endogenous sequence.

15 18. The method of claim 14 wherein said sequence XRY is a non-endogenous sequence.

19. A compound directly identified by the method of claim 1.

20. A compound directly identified by the method of claim 2.

21. A compound directly identified by the method of claim 3.

22. A compound directly identified by the method of claim 4.

20 23. A compound directly identified by the method of claim 5.

24. A compound directly identified by the method of claim 6.

25. A compound directly identified by the method of claim 14.

26. A pharmaceutical composition comprising a compound of claim 19.

27. A pharmaceutical composition comprising a compound of claim 20.

28. A pharmaceutical composition comprising a compound of claim 21.

29. A pharmaceutical composition comprising a compound of claim 22.

30. A pharmaceutical composition comprising a compound of claim 23.

31. A pharmaceutical composition comprising a compound of claim 24.

5 32. A pharmaceutical composition comprising a compound of claim 25.

33. A method for directly identifying a candidate compound as a compound selected from the group consisting of an inverse agonist, a partial agonist and an agonist to a non-endogenous constitutively activated G protein coupled cell surface orphan receptor comprising the steps of:

(a) contacting a candidate compound with a non-endogenous constitutively activated G protein coupled cell surface orphan receptor; and

(b) determining, by measurement of the compound efficacy at said contacted receptor, whether said compound is an inverse agonist, a partial agonist or an agonist of said receptor.

15 34. The method of claim 33 wherein the compound is determined to be an inverse agonist to said receptor.

35. A compound directly identified by the method of claim 33.

36. A compound directly identified by the method of claim 34.

37. A pharmaceutical composition comprising a compound of claim 35.

20 38. A pharmaceutical composition comprising a compound of claim 36.

39. A method for directly identifying a candidate compound as a compound selected from the group consisting of an inverse agonist, a partial agonist and an agonist to an endogenous constitutively activated G protein coupled cell surface orphan receptor comprising the steps of:

Sub B2
Sub B3

*Dist
B3
CDAT
5*

- (a) contacting a candidate compound with an endogenous constitutively activated G protein coupled cell surface orphan receptor; and
- (b) determining, by measurement of the compound efficacy at said contacted receptor, whether said compound is an inverse agonist, a partial agonist or an agonist of said receptor.

40. The method of claim 39 wherein the compound is determined to be an inverse agonist to said receptor.

41. A compound directly identified by the method of claim 39.

42. A compound directly identified by the method of claim 40.

10 43. A pharmaceutical composition comprising a compound of claim 41.

44. A pharmaceutical composition comprising a compound of claim 42.

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